

(19) World Intellectual Property
Organization
International Bureau



(43) International Publication Date
1 September 2005 (01.09.2005)

PCT

(10) International Publication Number
WO 2005/080355 A1

(51) International Patent Classification⁷: **C07D 253/08**,
237/26, 237/28, 237/30, A61K 31/502, 31/5025, 31/53,
A61P 25/28

PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM,
ZW.

(21) International Application Number:
PCT/US2005/004194

(84) Designated States (*unless otherwise indicated, for every
kind of regional protection available*): ARIPO (BW, GH,
GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM,
ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM),
European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI,
FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO,
SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG).

(22) International Filing Date: 9 February 2005 (09.02.2005)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
60/544,057 12 February 2004 (12.02.2004) US

(71) Applicant (*for all designated States except US*): **NEURO-
GEN CORPORATION** [US/US]; 35 Northeast Industrial
Road, Branford, CT 06405 (US).

(71) Applicants and

(72) Inventors: **XU, Yuelian** [CN/US]; 48 Highland Avenue,
East Haven, CT 06513 (US). **HAN, Bingsong** [CN/US];
55 North Avenue, North Haven, CT 06473 (US). **XIE,
Linghong** [US/US]; 136 Renee's Way, Guilford, CT 06437
(US). **MAYNARD, George** [US/US]; 27 Glenwood Road,
Clinton, CT 06413 (US).

(74) Agents: **KADLECEK, Ann** et al.; Neurogen Corporation,
35 Northeast Industrial Road, Branford, CT 06405 (US).

(81) Designated States (*unless otherwise indicated, for every
kind of national protection available*): AE, AG, AL, AM,
AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE,
KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD,
MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG,

Declarations under Rule 4.17:

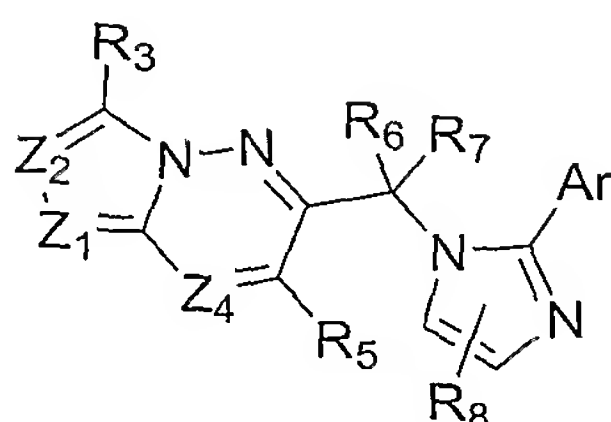
- *as to applicant's entitlement to apply for and be granted
a patent (Rule 4.17(ii)) for the following designations AE,
AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ,
CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE,
EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,
JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA,
MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM,
PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA,
ZM, ZW, ARIPO patent (BW, GH, GM, KE, LS, MW, MZ,
NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT,
BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR,
HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK,
TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ,
GW, ML, MR, NE, SN, TD, TG)*
- *as to the applicant's entitlement to claim the priority of the
earlier application (Rule 4.17(iii)) for all designations*

Published:

- *with international search report*

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: IMIDAZO-PYRIDAZINES, TRIAZOLO-PYRIDAZINES AND RELATED BENZODIAZEPINE RECEPTOR LIG-
ANDS



(I)

(57) Abstract: Compounds of the Formula are provided, as are methods for their preparation. The variables Z₁, Z₂, R₃, Z₄, R₅, R₆, R₇, R₈ and Ar in the above formula are defined herein. Such compounds may be used to modulate ligand binding to GABA_A receptors in vivo or in vitro, and are particularly useful in the treatment of a variety of central nervous system (CNS) disorders in humans, domesticated companion animals and livestock animals. Compounds provided herein may be administered alone or in combination with one or more other CNS agents to potentiate the effects of the other CNS agent(s). Pharmaceutical compositions and methods for treating such disorders are provided, as are methods for using such ligands for detecting GABA_A receptors (e.g., receptor localization studies).

WO 2005/080355 A1